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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/765,061 | 01/17/2001 | Melanie M. Sohocki | 25630/16UTL | 7715 |

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| EXAMINER | |
|---|---|
| SHIBUYA, MARK LANCE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/765,061 | SOHOCKI ET AL. | |
| | Examiner | Art Unit | |
| | Mark L. Shibuya | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-8,14-20,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13,21-24 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/5/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-27 are pending. Claims 1-8, 14-20, 25 and 26 are withdrawn from consideration. Claims 9-13, 21-24 and 27 are examined.

### *Election/Restrictions*

2. Applicant's election with traverse of Group IV, claims 9-13, 21-24 and 27, and in particular, now drawn to the mutation Trp278X, in the reply filed on 7/6/2006, is acknowledged. The traversal is on the ground(s) that that all recited mutations are mutations of the AIPL1 encoding or regulatory sequence, and the databases are such that the search should not represent a burden as the searches are now highly automated. Also the mutations are specific and represent a location of sites in the AIPL1 encoding or regulatory sequence that represent potentially signatures of a retinal disease, which can occur individually or collectively. Thus, applicant argues that a search for one mutation may well additionally identify other members of the same group. Applicant request that if a generic claim is deemed patentable for the Trp278X mutant, then the examiner search and examine all other non-elected inventions, as required by the MPEP.

This is not found wholly persuasive because the different mutations represent materially different nucleic acid/protein sequence variants of the AIPI1 gene/protein. Applicant does not argue that these sequences are obvious over one another.

The Requirement for Restriction/Election, mailed 4/12/2006, stated that the mutants selected from the group consisting of Ala336.DELTA.2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I, P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT.fwdarw.TGA), Val33ins 8 bp (GTGATCTT), Leu257del 9 bp (CTCCGGCAC), where considered to be each distinct inventions, as they represented materially different sequence of nucleotides and amino acids. Thus the said Requirement did not consider these mutants to be species but rather considered them to be distinct inventions.

The art and specification indicates that these mutations can be associated with different families, and so have apparently etiology and pathogenesis. Thus these mutation Inventions appear to be distinct, in that they have materially different modes of operation, function and effect.

Furthermore, if these mutations are claimed as sequences subject to the nucleotide/amino acid sequence rules, then as directed in MPEP 803.04, examination is limited to a reasonable number, which is generally considered to be less than ten. The number of mutations claimed number more than ten.

Finally, the examiner respectfully finds that the elected mutation of Trp278X, is anticipated in the prior art. See below rejections.

The examiner is willing to consider more particular reasons as to why the mutations would not constitute an undue administrative burden, in view of these specific considerations.

3. Claims 1-8, 14-20, 25 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/6/2006.

***Priority***

4. This application was filed 1/17/2001, which is the effective filing date.

***Information Disclosure Statement***

5. The information disclosure statement filed 11/05/2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citation to Hameed et al. (3/2000) and to Sohocki et al (1/2000) journal source information. The IDS has been placed in the application file, but the information referred to therein in regard to said references of Hameed et al. (3/2000) and Sohocki et al (1/2000) have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

### *Oath/Declaration*

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

### *Specification*

7. Applicants disclose nucleotide sequences in the drawings, particularly Figures 1 and 9, that must be identified by a SEQ ID number, pursuant to 37 CFR 1.821(d), which states: "Where the description or claims of a patent application discuss a sequence listing that is set forth in the 'Sequence Listing' in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." The identification of the sequences by SEQ ID numbers may be in the Brief Description of the Figures; or in the drawings themselves.

### *Claim Rejections - 35 USC § 112*

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 9-13 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for lack of written description.

Claim 9-13 are drawn to a method to determine if an animal has a retinal disease or has a propensity to pass a retinal disease to offspring, comprising the steps of: (A) extracting polynucleotide from a cell or sample; (B) determining if the polynucleotide contains a mutation in an AIPLI encoding or regulating region; and (C) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring.

Claim 27 is drawn to a method to determine if a cell or sample has an APL1 mutation comprising: (A) extracting polynucleotide from a cell; (B) amplifying polynucleotides which encode APL1; and (C) determining if the polynucleotide contains a Trp278X mutation; (D) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring.

The instant specification, at p. 13, lines 13-18, discloses retinal diseases and disorders as including Leber's congenital amaurosis, juvenile retinitis pigmentosa (RP), dominant cone-rod dystrophy, and other inherited and/or acquired retinopathies. The instant specification, at p. 13, lines 13-18, states that the present invention can be used as a diagnosis and/or treatment of inherited and/or acquired retinopathies in animals including humans and/or development of animal models for diseases caused by or

related to mutation in AIPL1. Thus the claim term retinal diseases broadly encompasses inherited and acquired retinopathies.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

One of skill in the art cannot envision the genus of retinal diseases that may be determined by detecting a mutation to an AIPL1 gene. The specification provides that Leber's congenital amaurosis may be so detected, but the instant specification does not provide the mutant genes or proteins that are capable of inducing any retinal disease, other than Leber's congenital amaurosis. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The mutant genes are required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only Leber's congenital amaurosis, but not the full breadth of the claims encompassing any retinal disease, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (sée page 1115).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

11. Claims 9-13, 21-24 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites the limitation "a retinal disease" in lines 2 and 7. There is uncertain antecedent basis for this limitation in the claim because it is not clear if this is the same as "a retinal disease", in line 1.

Claim 21 recites the limitation "in step (b)" in line 4-5 and "step (e)" in line 11. There is insufficient antecedent basis for these limitations in the claim.

Claim 22 recites the limitation "a patient" in 1. There is uncertain antecedent basis for this limitation in the claim because it is not clear if this patient describes the same patient of "a patient sample", in claim 21, lines 1-2.

Claim 27 recites the limitation "a cell" in line 3. There is uncertain antecedent basis for this limitation in the claim because it is not clear if this is the same as "a cell", in line 1.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 9-13, 21-24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Sohocki et al., Nature Genetics, Jan. 1, 2000, Vol. 24, pp. 79-83.

The claims, (as in claim 9 et seq.), are drawn to a method to determine if an animal has a retinal disease or has a propensity to pass a retinal disease to offspring, comprising the steps of: (A) extracting polynucleotide from a cell or sample; (B) determining if the polynucleotide contains a mutation in an AIPLI encoding or regulating region; and (C) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring; and variations thereof.

Also, the claims, (as in claim 21 et seq.), are drawn to methods for determining the presence of an APLI mutant in a patient sample, which comprises: (A) isolating polynucleotide extracted from the patient sample; (B) hybridizing a detectably labeled

oligonucleotide to the polynucleotide isolated in step (b), the oligonucleotide having at its 3' end at least 15 nucleotides complementary to a wild type polynucleotide sequence having at least one mutation; (C) attempting to extend the oligonucleotide at its 3'-end; (D) ascertaining the presence or absence of a detectably labeled extended oligonucleotide; and (E) correlating the presence or absence of a detectably labeled extended oligonucleotide in step (e) with the presence or absence of a AIPL1 Trp278X mutation; and variations thereof.

Also, the claims, (as in claim 27), are drawn to a method to determine if a cell or sample has an APL1 mutation comprising: (A) extracting polynucleotide from a cell; (B) amplifying polynucleotides which encode APL1; and (C) determining if the polynucleotide contains a Trp278X mutation; (D) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring; and variations thereof.

Sohocki et al., Nature Genetics, Jan. 1, 2000, Vol. 24, pp. 79-83, throughout the publication, and abstract disclose methods to determine if an animal has a retinal disease or has a propensity to pass a retinal disease to offspring, (see, e.g., Fig. 5), comprising the steps of: (A) extracting polynucleotide from a cell or sample, (e.g., p. 81, para 1); (B) determining if the polynucleotide contains a mutation in an AIPLI encoding or regulating region, (see e.g., Fig. 2, demonstrating mutant sequences, and p. 80, teaching elected mutation Trp278X); and (C) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring, (see, e.g., Fig. 5); and as in instant claims 9-13.

Sohocki et al., throughout the publication and in the abstract, disclose methods for determining the presence of an APLI mutant in a patient sample, including members of a Pakistani family, LCA4 family, which comprises: (A) isolating polynucleotide extracted from the patient sample; (B) hybridizing a detectably labeled oligonucleotide to the polynucleotide isolated, (see, e.g., Fig. 1), the oligonucleotide having at its 3' end at least 15 nucleotides complementary to a wild type polynucleotide sequence having at least one mutation, (see, e.g., Figure 2); (C) attempting to extend the oligonucleotide at its 3'-end, (see, e.g., Fig. 1, Methods Section, p. 81, para 4-5, p. 82, para 2, p. 83, para 2); (D) ascertaining the presence or absence of a detectably labeled extended oligonucleotide; and (E) correlating the presence or absence of a detectably labeled extended oligonucleotide with the presence or absence of a AIPL1 Trp278X mutation (see p. 80, para 1-6, Fig. 5); as in instant claims 21-24. Sohocki et al., in the abstract, teach taking a patient sample prior to isolation. Sohocki et al., at Fig. 1, and p. 81, para 6, teach amplification, hybridization, and fluorescence *in situ* hybridization (fluorochrome label), northern blot (radioisotope label), and digoxygenin *in situ* hybridization (enzyme label); as in instant claims 21-24.

Sohocki et al, throughout the publication, disclose method to determine if a cell or sample has an APL1 mutation comprising: (A) extracting polynucleotide from a cell; (B) amplifying polynucleotides which encode APL1; and (C) determining if the polynucleotide contains a Trp278X mutation; (D) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring; as in instant claim 27.

14. Claims 9, 12, 13 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Damji, et al., American Journal of Human Genetics, Oct. 2000, Vol. 67, No. 4 Supplement 2, pp. 382, Abstract 2142.

Damji, et al., throughout the abstract, teach a method to determine if a human patient, (understood here to encompass broadly "an animal", as in the claim) has a retinal disease or has a propensity to pass a retinal disease to offspring, comprising the steps of: (A) extracting polynucleotide from a cell or sample; (B) determining if the polynucleotide contains a mutation in an AIPL1 encoding or regulating region; and (C) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring; and wherein the determining is done via sequencing, (as in claim 12); and wherein the mutation is Trp278X, as in claim 13.

***Conclusion***

15. Claims 9-13, 21-24 and 27 are rejected.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark L. Shibuya
Examiner
Art Unit 1639